REMARKS

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 CFR §1.112, and in light of the remarks which follow are respectfully requested.

By the present amendments, the prior claims have been cancelled in favor of new claims 60-85. All of these claims find support in the original-filed claims.

Also, Applicants provide herewith Figures 1-4 which are described in this application, but which were inadvertently omitted on filing of this application. Applicants respectfully note that a telephone conference was held with Examiner Gambel. During this phone conference, the undersigned advised that these figures do not constitute new matter as they are fully described in this application and contain data that corresponds to experiments described in the examples. As evidence of this fact, Applicants are providing an affidavit by one of the inventors, Hari Hariharan, who attests to the fact that these figures are the same figures described in the as-filed application.

Turning now to the Office Action, claims 10-13, 18-27, 32-35 and 57-79 stand rejected under 35 USC §112, first paragraph. This rejection should be moot as the claims are now restricted to use of an anti-CD40L and anti-CD20 antibody or fragment thereof.

Claims 7-10, 12-13, 18-21, 33, 35 and 37 stand rejected as depending on the availability of a deposited cell line. This rejection is respectfully traversed to the extent it may apply to the claims as amended.

The only two unique antibodies referred to in the claims are Rituxan® and IDEC-131. Both of these antibodies are the subject of claims contained in issued or allowed patents which are incorporated by reference.

In fact, Rituxan® is widely commercially available for treatment of non-Hodgkin's lymphoma.

Likewise, IDEC-131 is a humanized anti-CD40L antibody disclosed in U.S. Serial No. 08/554,240, incorporated by reference in its entirety which stands allowed. If the Examiner would prefer, Applicants would be pleased to incorporate the full sequence of this humanized antibody from this application to remove this rejection, if necessary.

Also, Applicants would be willing to incorporate the ATCC accession number for the cell line that produces the Rituxan® antibody (patent that identifies this cell line, ATCC6902 deposited on September 4, 1992 is disclosed in this application). While

Applicants, however, believe that this should not be necessary (as U.S. Patents 5,776,456 and 5,843,849 incorporated by reference fully disclose this antibody and establish its public availability (see pages 42 and 43 of the subject application)).

The other §112, second paragraph rejections are moot as the new claims do not suffer from the same defects.

Claims 1-2, 6-13, 18-27, 32-36, and 57-59 stand rejected based on 35 USC §103(a) as being unpatentable over Kaminski, Anderson et al., in view of Smiers et al., Schattner et al., Gruss et al., Renard et al., Black et al., and Noelle et al., in view of standard chemotherapeutic treatments. This rejection is respectfully traversed.

Essentially, all the primary references teach the use of anti-CD20 antibodies to treat B cell malignancies including B cell leukemia and B cell lymphoma. The Examiner acknowledges that these reference do not suggest the use of anti-CD40L antibodies in combination therewith.

However, the Examiner cites Smiers et al., Schattner et al., Gruss et al., and Renard et al., which teach that it was known at the time of invention that B cell leukemias expressed CD40 and CD20 antigen, and notes that Gruss et al. disclosed the use of CD40L antibodies to inhibit malignant B cell growth.

This is acknowledged, however Applicants respectfully advise that none of the references, including Black et al., Gruss et al., or Noelle et al., suggest combined use of an anti-CD40L antibody and an anti-CD20 antibody to treat a B cell leukemia as claimed.

While Applicants agree that combination therapies are routinely used in treating malignancy, this generally applies to the combined use of radiotherapy or chemotherapy, not the combined administration of different antibodies. To Applicants' knowledge, this would constitute the first known therapeutic treatment of a leukemia with two different antibodies. In fact, Rituxan® is the first antibody that was approved for treatment of any B cell malignancy which attests to the unpredictabilities associated with use of antibodies for therapy, and especially treatment of B cell malignancies.

Also, Applicants separately argue the patentability of claims that require the inclusion of chemotherapy. As disclosed in the examples, Applicants have demonstrated that treatment with an anti-CD40L antibody, and particularly IDEC-131, as well as Rituxan® renders malignant B cells more susceptible to the effects of chemotherapeutic agents (adriamycin exemplified).

Applicants respectfully submit that claims directed to combined use of anti-CD40L antibody, anti-CD20 antibody and chemotherapy should at least be allowed as no reference would fairly suggest that treatment with anti-CD40L antibody would render malignant B cells more susceptible to the effect of chemotherapy. Thus, synergistic benefits are achieved by Applicants' therapeutic regimen which are not fairly suggested by the prior art.

Based thereon, withdrawal of the §103 rejection of claims 1-2, 6-13, 18-27, 32-36, and 57-59 is respectfully requested.

Finally, claims 1-2, 6-13, 18-27, 32-36, and 57-59 stand rejected on obviousness double-patenting grounds. This rejection will be overcome by a Terminal Disclaimer upon indication that this application is otherwise allowable.

Based on the foregoing, this application is believed to be otherwise in condition for allowance. A notice to that effect is respectfully solicited.

Respectfully submitted,
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